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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/886,400	06/20/2001	Dennis Murphy	DIVER1120-4	4902

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FISH & RICHARDSON, PC
4350 LA JOLLA VILLAGE DRIVE
SUITE 500
SAN DIEGO, CA 92122

EXAMINER
RAMIREZ, DELIA M

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 03/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/886,400	MURPHY ET AL.	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *93-119* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *104* is/are allowed.

6)☒ Claim(s) *93-103, 105-119* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 December 2002* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *18* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Application

Claims 93-119 are pending.

Applicant's cancellation of claims 1-92 and addition of claims 93-119 in Paper No. 16, filed on 12/23/2002 is acknowledged.

Applicant's submission of a declaration under 37 CFR 1.132 by Mr. Walter Callen, an ATCC international form indicating the deposit of plasmid 18GC, a declaration by Ms. Mi Kim in regard to a biological deposit made under the terms of the Budapest Treaty, a copy of the assignment, and a new sequence listing, in Paper No. 16, filed on 12/23/2002 is acknowledged.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Information Disclosure Statement

1. The information disclosure statement (IDS) submitted on 1/28/2003 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Terminal Disclaimer

2. The terminal disclaimer filed on 12/23/2002 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U.S. Patent No. 5958751 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Priority

3. Applicants have indicated in page 13, first paragraph, of the response filed on 12/23/2002, that upon re-sequencing of plasmid 18GC, 5 nucleotide discrepancies were found which resulted in one amino acid change. It is noted, however, that no amino acid changes could be found in the new sequence listing filed. The Examiner has found in related U.S. Application No. 10/114,083 a supplemental reply which indicates that no amino acid changes resulted from the 5 nucleotide discrepancies (page 2, second paragraph). For examination purposes, it will be assumed that no amino acid changes resulted from the re-sequencing of plasmid 18GC. Applicants are requested to clarify this matter in response to this Office Action.

Drawings

4. Figure 5A is objected to because Figure 5A, as amended, now shows the first codon, TTG, as encoding an Ile residue instead of a Leu residue. Since TTG encodes Leu and not Ile, it is assumed that the recitation of Ile in Figure 5A is a typographical error and not an amino acid change. Correction is required.

5. The formal drawings submitted on 12/23/2002 have been reviewed by a draftsperson.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 94, 105-115, 118-119 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claim 94 (claims 105-115, 118-119 dependent thereon) are indefinite in the recitation of "about 50% sequence homology" for the following reasons. The term "about" is a relative term and neither the specification nor the claim provide a standard for ascertaining the requisite degree, therefore one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is noted that the term "about 50%" implies a range of values which can be higher and/or lower than 50%. As such, in the absence of a defined range, one cannot establish which is the lowest % sequence homology and/or the highest % sequence homology encompassed by the claims. For examination purposes, the term "about 50% sequence homology" will be interpreted as "50% sequence homology". Correction is required.

9. Claim 94 is indefinite in the recitation of "The purified polypeptide" as there is no antecedent basis for "the purified polypeptide". The term "the" within the context of the claim is equivalent to "one" which is confusing since more than one polypeptide could have the recited characteristics. Correction is required.

Claim Rejections - 35 USC § 112, First Paragraph

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 105-115 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

12. This rejection, which has been discussed at length in Paper No. 10, 6/18/2002, was applied to cancelled claims 24-35, 86-87 and is now applied to newly added claims 105-115 for the reasons of record.

13. Applicants argue that the new claims are now directed to polypeptides having α-galactosidase activity, therefore no longer directed to polypeptides of any function. In addition, Applicants argue that the specification sufficiently describes the claimed invention and that the skilled artisan is well versed in protocols used in the laboratory for biological research. In particular, Applicants argue that the specification teaches how to assess percent homologies and provides an assay to test for activity. Since the specification teaches how to test for activity, Applicants assert that isolating polypeptides which are thermostable after exposure to temperatures of 60-105 C is fully described.

14. Applicant's arguments have been fully considered but are not deemed persuasive to avoid the rejection on newly added claims 105-115. While the Examiner acknowledges that (1) the instant claims now recite a specific function for the claimed polypeptides, (2) a test for activity is provided in the specification, (3) assessing percent homology is well known in the art, and (4) a skilled artisan is well versed in protocols used for biological research, the instant claims are not adequately described for the following reasons. The claims are directed to genera of polypeptides which have α-galactosidase activity and comprise between 10 to 150 consecutive

amino acid residues of 50%-100% sequence homologs of the polypeptide of SEQ ID NO: 4. An adequate description of a genus of polypeptides may be achieved by a recitation of a representative number of polypeptides defined by their amino acid sequence or a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. The recited structural feature of the genera (i.e. polypeptide comprising 10-150 consecutive amino acids of a sequence only 50% homologous to SEQ ID NO: 4) does not constitute a substantial portion of the genera since the remainder of the structure of any polypeptide having α-galactosidase activity is completely undefined and the specification does not provide the remaining structural features necessary for members of the genera to be selected. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed. Applicants are referred to the revised guidelines concerning compliance with the written description requirement of 35 USC 112, first paragraph, published in the Official Gazette and also available at the USPTO website.

15. Claims 93-103, 105-119 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polypeptide of SEQ ID NO: 4, which is encoded by the polynucleotide of SEQ ID NO: 3, does not reasonably provide enablement for (1) any polypeptide comprising at least 50-95% sequence homology to the polypeptide of SEQ ID NO: 4, (2) any polypeptide comprising at least 10-150 consecutive amino acids of the polypeptide of SEQ ID NO: 4 or homologs thereof as encompassed by the claims, or (3) compositions comprising the polypeptides as described in (1) or (2). The specification does not enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

16. This rejection, which has been discussed at length in Paper No. 10, 6/18/2002, was applied to cancelled claims 24-35, 64, 86-87 and is now applied to newly added claims 93-103, 105-119 for the reasons of record.

17. Applicant's argue that the specification discloses the amino acid sequence of a novel polypeptide having α–galactosidase activity. Furthermore, Applicants argue that at the time the application was filed, the state of the art and level of skill of the artisan in molecular biology was very advanced, therefore one of skill in the art can use the disclosure provided, well known properties such as thermostability, and well known laboratory techniques to create thermostable polypeptides (1) having at least 70% sequence identical to the polypeptide of SEQ ID NO: 4 and (2) having at least 10 consecutive amino acids of the polypeptide of SEQ ID NO: 4 or its variants. In addition, according to Applicants, the disclosure provides an exemplary assay for testing the polypeptides for activity. In regard to undue experimentation, Applicants argue that while many constructs may need to be created/isolated and analyzed to isolate the claimed polypeptides, this does not constitute undue experimentation since the procedures for isolating such polypeptides are widely accepted, routine protocols. In view of these arguments, Applicants conclude that the rejection based upon 35 USC 112, first paragraph is not applicable to the newly added claims.

18. Applicant's arguments have been fully considered but are not deemed persuasive to avoid the rejection applied to newly added claims 93-103, 105-119. While it is agreed that it is not undue experimentation to detect α-galactosidase activity and that a skill artisan can create many

constructs using well-known molecular biology techniques, it is not routine experimentation to randomly create an infinite number of variants and test them for activity. Instead, a skilled artisan would require some knowledge or guidance as to which structural elements (i.e. amino acid residues) correlate with α-galactosidase activity within the polypeptide of SEQ ID NO: 4 and which structural elements correlate with thermostability of the protein, before creating variants and testing them for activity. As indicated in previous Office Action Paper No. 10, the state of the art teaches several examples where small changes in the structure of a polypeptide render polypeptides of different function. See the teachings of Bork (Genome Research, 10:398-400, 2000), Van de Loo et al. (Proc. Natl. Acad. Sci. 92:6743-6747, 1995) and Broun et al. (Science 282:1315-1317, 1998) already discussed. Further examples of how minimal changes in structure can lead to different function are described by Witkowski et al. (Biochemistry 38:11643-11650, 1999) and Seffernick et al. (J. Bacteriol. 183(8):2405-2410, 2001; cited in the IDS). Witkowski et al. teaches that one amino acid substitution transforms a β-ketoacyl synthase into a malonyl decarboxylase and completely eliminates β-ketoacyl synthase activity. Seffernick et al. teaches that two naturally occurring Pseudomonas enzymes having 98% amino acid sequence identity catalyze two different reactions: deamination and dehalogenation, therefore having different function. In the instant case, there is no disclosure of which are the critical structural elements that a polypeptide should have to display α-galactosidase activity nor there is disclosure of which amino acids can be substituted or deleted in the polypeptide of SEQ ID NO: 4 to obtain sequence homolog as recited in the claims and still retain α-galactosidase activity. In view of the amount of information provided, the lack of relevant examples, the lack of knowledge about the critical structural elements required to maintain α-galactosidase function

and thermostability, and the state of the art in regard to the unpredictability of assigning function based on sequence homology, one of skill in the art would have to go through the burden of undue experimentation to practice the full scope of the claimed invention.

Claim Rejections - 35 USC § 102

19. Claims 24-35 and 64 were rejected under 35 U.S.C. 102(b) as being anticipated by Kawarabayasi et al. (PIR accession number E71144, August 14, 1998).

20. This rejection was discussed at length in Paper No. 10, mailed on 6/20/2002.

21. Applicants argue that the instant application is entitled to priority back to March 8, 1996, which is the filing date of U.S. Application No. 08/613,220. Applicants assert that the plasmid 18GC was disclosed in U.S. Application No. 08/613,220 and submit an amended sequence listing from re-sequenced clone 18GC, which was deposited at ATCC on 9/10/2002.

22. It is noted that according to PTO's sequence databases, the polypeptide of SEQ ID NO: 4 claimed in U.S. Application No. 08/613,220 is not the same polypeptide as that of the instant application. The polypeptide of SEQ ID NO: 4 in the instant application is 364 amino acids in length, whereas the polypeptide of SEQ ID NO: 4 in U.S. Application No. 08/613,220 (now U.S. Patent No. 5958751) is only 346 amino acids in length. See sequence listing in U.S. Patent No. 5958751. Therefore, a sequence search of the polypeptide of the instant application indicated that the polypeptide of U.S. Application No. 08/613,220 and the polypeptide of the instant application are 84% sequence identical. The 102(b) rejection was applied due to the fact that according to PTO's databases, SEQ ID NO: 4 of the instant application was not disclosed in U.S. Application No. 08/613,220.

It appears that Figure 1 of U.S. Patent No. 5958751 (SEQ ID NO: 4 according to such patent) discloses a polypeptide of 364 amino acids, based upon visual comparison of Figure 5 as originally filed in the instant application and Figure 1 of such patent. While visual comparison of Figure 5 as originally filed in the instant application and Figure 1 of such patent appear to indicate that both figures are identical, the Examiner cannot solely rely on such visual comparison to conclude that the sequence disclosed in Figure 1 of U.S. Patent No. 5958751 and that of SEQ ID NO: 4 of the instant application are the same unless an alignment of both sequences is performed. However, in view of the disclosure of clone 18GC in U.S. Application No. 08/613,220 (now U.S. Patent No. 5958751), the submission of Mr. Walter Callen's declaration, an ATCC international form indicating the deposit of plasmid 18GC, and a declaration by Ms. Mi Kim in regard to a biological deposit made under the terms of the Budapest Treaty, and the amended sequence listing, it has been determined that the polypeptide of SEQ ID NO: 4 of the instant application is entitled to claim priority back to March 8, 1996, which is the filing date of U.S. Application No. 08/613,220. Thus, this rejection is hereby withdrawn.

Claim Rejections - 35 USC § 103

23. Claims 86-87 were rejected under 35 U.S.C. 103(a) as being unpatentable over Kawarabayasi et al. (PIR accession number E71144, August 14, 1998).

24. This rejection was discussed at length in Paper No. 10, mailed on 6/20/2002.

25. Applicant's arguments in regard to this rejection have been summarized above. See claims rejections under 35 USC 102.

26. This rejection is hereby withdrawn for the reasons set forth above. See claim rejections under 35 USC 102.

Double Patenting

27. Claims 24-35, 64 and 86-87 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 15 of U.S. Patent No. 5958751.

28. While claims 24-35, 64 and 86-87 have been cancelled, this rejection would have been applied to newly added claims 93-103, 105-119, however in view of Applicant's submission of a terminal disclaimer, this rejection is hereby withdrawn.

29. Claims 24-35, 64 and 86-87 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 10-11 of copending Application No. 09/407806.

30. While claims 24-35, 64, and 86-87 have been cancelled, this rejection would have been applied to newly added claims 93-119. However, in view of cancellation of claims 10-11 in copending Application No. 09/407806, this rejection is hereby withdrawn.

Allowable Subject Matter

31. Claim 104 appears to be allowable over the prior art of record.

Conclusion

32. Applicant's amendment, which canceled claims 1-92 and added claims 93-119, necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

33. Applicants are requested to submit a clean copy of the pending claims (including amendments, if any) in future written communications to aid in the examination of this application.

34. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 308-4556. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE

COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (703) 306-0288. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
March 14, 2003

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1900~~ 1600